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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/466,921	06/06/95	ALTZUN N	03459.0008-U

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EXAMINER	
PARKIN, J	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 10/28/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/466,921	Alizon et al.
Examiner	**Group Art Unit**
Jeffrey S. Parkin, Ph.D.	1648

☒ Responsive to communication(s) filed on *16 Jul 1999* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *39-52 and 60-73* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *39-52, 60, and 61* is/are allowed.

☒ Claim(s) *62-73* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Amendment

Status of the Claims

1. Acknowledgement is hereby made of the Amendment submitted 16 July, 1999, wherein claims 53-59 were canceled without prejudice or disclaimer, claim 60 amended, and new claims 62-73 submitted. Claims 39-52 and 60-73 are pending in the instant application.

35 U.S.C. § 112, First Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The previous rejection of claims 53-61 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is moot in view of applicants' amendment.

4. The previous rejection of claims 53-61 under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, is moot in view of applicants' amendment.

New Grounds of Rejection

35 U.S.C. § 112, Second Paragraph

MT 5. Claims 68 and 69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The reference to "amplified" copies of HIV-1 DNA fragments is vague and indefinite since the nature of the amplification is not provided. For instance, are the claims directed toward PCR amplified HIV-1 fragments (which are clearly not supported by the disclosure) or do they encompass some other amplification process (i.e., the amplification and plaque purification of a lambda phage clone containing an HIV-1 insert). Appropriate amendment of the claim language, as supported by the disclosure, is required.

35 U.S.C. § 112, First Paragraph

MT 6. New claims 62-73 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). Applicants have submitted claims (63-67 and 70-73) directed toward HIV-1 DNA fragments that hybridize to HIV-1 genomic DNAs under non-stringent hybridization conditions comprising 20% formamide, 8X SSC, at a temperature 37°C, followed by washing conditions of 2X SSC, 0.1% SDS, at a temperature 37°C. New claims 68 and 69 are directed toward amplified copies of HIV-1 DNA fragments suitable as probes under the recited conditions. As previously noted, although the disclosure describes similar hybridization conditions to those

claimed by applicants, these conditions were discussed in reference to hybridization assays performed between three isolated LAV cDNA clones (e.g., λJ19, λJ27, and λJ81) and cloned HTLV-II DNA (see pages 11 and 12 of the disclosure). **Thus, the purpose of this hybridization assay was to assess the genetic relatedness of the recently identified LAV cDNA clones to that of other known retroviruses (e.g., HTLV-II).** Moreover, the claims encompass an exceedingly large genus of nucleic acids encompassing small fragments from 10-15 nt to full-length proviral genomes (~10 kb). However, **the disclosure fails to describe any other nucleic acids with the exception of those specific λJ19, λJ27, and λJ81 restriction fragments provided. The disclosure does not provide restriction maps or nucleotide sequences from any other HIV-1 isolate. The disclosure does not describe hybridization assays involving λJ19 restriction fragments and other HIV-1 clones.** Moreover, the disclosure fails to describe the preparation of amplified DNA fragments. Accordingly, the skilled artisan, upon perusal of the specification, would not reach the conclusion that applicants' contemplated isolating and purifying other HIV-1 fragments that hybridize under the precise conditions claimed. Accordingly, applicants have not met their burden pertaining to this aspect of § 112. See also *Bigham* v. *Godtfredsen*, 857 F.2d 1415, 8 U.S.P.Q.2d 1266 (Fed. Cir. 1988), wherein the court concluded that the disclosure of an earlier compound was insufficient to provide an adequate written description for later claimed variants of this compound. Applicants submit that an adequate written description is provided by the disclosure. These arguments are not deemed persuasive for the reasons note above.

W.D.7. Newly submitted claims 62-73 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Newly submitted claims 62-73 are directed toward any HIV-1 DNA fragment that is capable of hybridizing to HIV-1 genomic DNA under the claimed hybridization conditions. These claims encompass nucleic acids obtained from any HIV-1 isolate of greatly differing sizes (i.e., a small restriction fragment of 100 nt would be capable of hybridizing, as well as, a proviral insert (~10 kb) released from a cloning vector). The disclosure provides preliminary restriction maps of LAV cDNA (e.g., pLAV75, pLAV82 and pLAV13) and lambda phage clones (e.g., λJ19 and λJ81) (refer to Figures 1 and 2). The restriction coordinates are disclosed on page 4, as well as a series of restriction fragments believed to correspond to the *gag*, *pol* and *env* coding regions (e.g., *Pst*I (800 nt)/*Kpn*I (3500 nt); *Kpn*I(3,500 nt)/*Bgl*II (6,500 nt); *Kpn*I (6,100)/*Bgl*II (9150)). The specification does not disclose, *ipsis verbis*, HIV/LAV viral clones or restriction fragments obtained from any other viral isolate that are capable of hybridizing under the claimed, or any other conditions.

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate

guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide an adequate written description of nucleic acids obtained from any other HIV-1 isolate, with the exception of the identified LAV restriction fragments. The specification only details the isolation of a small number of lambda phage clones all corresponding to the same viral isolate, LAV-1. However, the specification is silent pertaining to the identification and molecular characterization of any other HIV-1 isolates.

2) The disclosure fails to provide a sufficient number of working embodiments to enable the breadth of the claimed invention. As discussed in the preceding section, the disclosure only details the identification and preliminary restriction analysis of a small number of lambda phage clones derived from a single HIV-1 isolate designated LAV. The disclosure is silent pertaining to the inclusion of working examples detailing the identification and preliminary characterization of any single HIV-1 isolate other than LAV.

3) The prior art teaches that the *Lentivirinae* exist as a quasispecies and display considerable genotypic variability (Goodenow *et al.*, 1989; Holland *et al.*, 1992; and Gao *et al.*, 1994). Accordingly, the skilled artisan cannot, *a priori*, predict the restriction map or nucleotide sequence of any given HIV-1 isolate.

4) The breadth of the claimed invention encompasses an exceedingly large genus of nucleic acids that are simply not supported by the disclosure. The mere recitation of a small number of species is insufficient to provide adequate support for a large genus of compounds, particularly in arts where considerable unpredictability exists. *Bigham* v. *Godtfredsen*, 857 F.2d 1415, 8 U.S.P.Q.2d 1266 (Fed. Cir. 1988). *Fujikawa v. Wattanasin*, 39 U.S.P.Q.2d 1895

(C.A.F.C 1996). *University of California v. Eli Lilly and Co.*, 39 U.S.P.Q.2d 1225 (D.C. S.Ind. 1995).

5) Legal precedence dictates that nucleic acids must be precisely defined in the disclosure by the provision of sufficient structural and functional characteristics. *Fiers* v. *Revel*, 984 F.2d 1164, 25 U.S.P.Q.2d 1601 (Fed. Cir. 1993). *Fujikawa v. Wattanasin*, 39 U.S.P.Q.2d 1895 (C.A.F.C 1996). *University of California v. Eli Lilly and Co.*, 39 U.S.P.Q.2d 1225 (D.C. S.Ind. 1995). However, the disclosure is deficient as it pertains to a description of these structural characteristics.

Applicants traverse and submit, *inter alia*, that the claimed invention is fully enabled by the disclosure and that the Office has failed to establish a *prima facie* case for lack of enablement. Applicants' arguments have been duly noted but are not deemed to be persuasive. Applicants also note that a number of post-filing date references were relied upon, which is inappropriate. Applicants are reminded that although it is generally preferred that the submission of pre-filing date, or effective filing date, references should be provided to support a *prima facie* demonstration of lack of enablement, nonetheless, it is also acceptable to submit later-dated references if they provide evidence as to what was known on or before the effective filing date of the application. Thus, if individuals skilled in the art state that a particular invention is not feasible after the filing date of the claimed invention, that would be sufficient evidence that the invention was not possible at the time of filing. Moreover, the court decided in *In re Budnick*, 190 U.S.P.Q. 422 (C.C.P.A. 1976), that the argument of counsel cannot take the place of evidence. Contrary to applicants' arguments, the examiner has set forth several legitimate scientific caveats that would preclude practice of the claimed invention. However, applicants have not provided sufficient scientific

evidence to rebut the enablement rejection. Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation to practice the claimed invention.

Allowable Subject Matter

8. Claims 39-52, 60, and 61 appear to be free of the prior art and are allowable.

Finality of Office Action

9. Applicant's amendment necessitated any and all new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Correspondence

10. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax

number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

11. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Anthony Caputa, Ph.D., or Laurie Scheiner, can be reached at (703) 308-3995 or (703) 308-1122, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

09 October, 1999

LAURIE SCHEINER
PRIMARY EXAMINER